



**NTP**

National Toxicology Program

# **Report on the National Toxicology Program Technical Reports Peer Review Panel Meeting October 29, 2013**

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**National Institute of Environmental Health Sciences**

**NTP Board of Scientific Counselors Meeting**

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# National Toxicology Program (NTP) Technical Reports

- NTP conducts rodent toxicity and cancer studies on agents of public health concern to identify potential hazards for human health
- NTP technical reports describe the methods, results, and NTP conclusions as “levels of evidence” for carcinogenic activity under the specific conditions of the study

# Levels of Evidence of Carcinogenic Activity

**Clear evidence:** Dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy

**Some evidence:** Chemical-related increased incidence of neoplasms in which the strength of the response is less than that required for clear evidence

**Equivocal evidence:** Marginal increase of neoplasms that may be chemical related

**No evidence:** No increase of neoplasms attributed to chemical

**Inadequate study:** Flaws preclude interpretation

# Draft Technical Reports Peer Reviewed on October 29, 2013

- Cobalt Metal Dust (TR-581)
- Vinylidene Chloride (TR-582)
- Tetrabromobisphenol-A (TR-587)
- Glycidamide (TR-588)

# Technical Reports Peer Review Panel

- John Cullen, VMD, PhD, North Carolina State University (Panel Chair)
- Norman Barlow, DVM, PhD, MBA, MLD, DAVCP, DABT, Sanofi
- Russell Cattley, VMD, PhD, DACVP, Auburn University
- Deborah Cory-Slechta, PhD, University of Rochester School of Medicine and Dentistry
- Terry Gordon, PhD, New York University Langone Medical Center
- Joel Parker, PhD, University of North Carolina
- Karen Regan, DVM, Research Pathology Services, LLC
- Timothy Zacharewski, PhD, Michigan State University
  
- Richard Miller, DVM, PhD, GlaxoSmithKline (BSC Liaison)

## Charge to the Panel

- Review and evaluate the scientific and technical elements of the study and its presentation
- Determine whether the study's experimental design, conduct, and results support the NTP's conclusions regarding the carcinogenic activity and toxicity of the substance tested

## Cobalt Metal Dust (TR-581)

- By-product in alloy production, cobalt salts, and nuclear technology
- The panel recommended accepting the conclusions as written (7 yes, 0 no, 0 abstentions)

| Sex/Species | Level of Evidence | Neoplastic Lesions                                                                                                   |
|-------------|-------------------|----------------------------------------------------------------------------------------------------------------------|
| Male Rats   | Clear             | Alveolar/bronchiolar adenoma and carcinoma in the lung, Benign and malignant pheochromocytoma of the adrenal medulla |
| Female Rats | Clear             | Alveolar/bronchiolar adenoma and carcinoma in the lung, Benign and malignant pheochromocytoma of the adrenal medulla |
| Male Mice   | Clear             | Alveolar/bronchiolar neoplasms of the lung (predominantly carcinoma)                                                 |
| Female Mice | Clear             | Alveolar/bronchiolar neoplasms of the lung (predominantly carcinoma)                                                 |

# Vinylidene Chloride (TR-582)

- Intermediate in synthesis of polymers
- The panel recommended accepting the conclusions as written (7 yes, 0 no, 0 abstentions)

| Sex/Species | Level of Evidence | Neoplastic Lesions                                                                   |
|-------------|-------------------|--------------------------------------------------------------------------------------|
| Male Rats   | Clear             | Malignant mesothelioma                                                               |
| Female Rats | Some              | C-cell adenoma or carcinoma in the thyroid gland, Systemic mononuclear cell leukemia |
| Male Mice   | Clear             | Renal tubule adenoma and carcinoma                                                   |
| Female Mice | Clear             | Systemic hemangioma or hemangiosarcoma (combined)                                    |

# Tetrabromobisphenol-A (TR-587)

- Flame retardant
- The panel recommended accepting the conclusions as written (4 yes, 1 no, 0 abstentions)

| Sex/Species | Level of Evidence | Neoplastic Lesions                                               |
|-------------|-------------------|------------------------------------------------------------------|
| Male Rats   | Equivocal         | Interstitial cell adenomas of the testis                         |
| Female Rats | Clear             | Uterine epithelial tumors (predominantly uterine adenocarcinoma) |
| Male Mice   | Some              | Hepatoblastoma                                                   |
| Female Mice | No Evidence       | -                                                                |

## Glycidamide (TR-588)

- Metabolite of acrylamide, a by-product of certain food preparations
- The panel recommended accepting the conclusions as written (6 yes, 1 no, 0 abstentions)

| Sex/Species | Level of Evidence | Neoplastic Lesions                                                                                                                                                                                                                                  |
|-------------|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Male Rats   | Clear             | Malignant mesothelioma of the epididymis and testis tunica, malignant schwannoma of the heart, follicular cell adenoma or carcinoma of the thyroid gland, and oral cavity (oral mucosa or tongue) papillomas or carcinomas                          |
| Female Rats | Clear             | Fibroadenomas of the mammary gland, oral cavity (oral mucosa or tongue) squamous cell papillomas or carcinomas, follicular cell adenoma or carcinoma of the thyroid gland, and carcinomas of the clitoral gland                                     |
| Male Mice   | Clear             | Adenoma of the Harderian gland, alveolar/bronchiolar neoplasms (primarily adenoma) of the lung, squamous cell neoplasms (primarily papilloma) of the skin, and squamous cell neoplasms (primarily papilloma) of the forestomach                     |
| Female Mice | Clear             | Adenoma of the Harderian gland, alveolar/bronchiolar neoplasms (primarily adenoma) of the lung, adenoacanthoma and adenocarcinoma of the mammary gland, squamous cell papilloma of the forestomach, and malignant mesenchymal neoplasms of the skin |

# Other Topics from the Review Meeting

- Change in Rat Stocks
  - F344/N to F344/NTac to Wistar Han
- Extended Evaluation of the Uterus
  - Tetrabromobisphenol A
- Molecular Analysis of Tumors
  - Cobalt Metal Dust: Alveolar/Bronchiolar Carcinomas of the Lung
  - Vinylidene Chloride: Mesotheliomas
  - Tetrabromobisphenol A: Adenocarcinomas of the Uterus

## Next Steps

- NTP Technical Reports to be published